HLA Region Genetics in Immune-Mediated Diseases

RFA Number: RFA-AI-04-039

Part I Overview Information

Department of Health and Human Services

Participating Organizations:
National Institutes of Health (NIH), (http://www.nih.gov/)

Components of Participating Organizations:
National Institute of Allergy and Infectious Diseases (NIAID), (http://www.niaid.nih.gov/)

Announcement Type:
New

Update: The following update relating to this announcement has been issued:

- July 31, 2009 - This RFA has been reissued as (RFA-AI-09-030).
- November 23, 2004 (NOT-AI-05-008) - NIAID is amending RFA-AI-04-039 with an addendum to the announcement.

Catalog of Federal Domestic Assistance Number(s): No. 93.856, Microbiology and Infectious Diseases Research
No. 93.855, Immunology, Allergy, and Transplantation Research

Key Dates
Release Date: September 28, 2004

Letters Of Intent Receipt Date(s): December 10, 2004

Application Receipt Dates(s): January 11, 2005
Peer Review Date(s): April, 2005 Council Review Date(s): June, 2005
Earliest Anticipated Start Date: July, 2005 Additional Information To Be Available Date (URL Activation Date): http://www.niaid.nih.gov/ncn/budget/QA/rfa-04-039.htm (October 1, 2004)
Expiration Date: January 12, 2005

Due Dates for E.O. 12372 Not Applicable

Executive Summary

Single institutions or consortia of institutions are invited to participate in a cooperative research group to define the association between human leukocyte antigen (HLA) region genes or genetic markers and immune-mediated diseases, including risk and severity of disease, and organ, tissue, and cell transplantation outcomes.

Approximately $2 million will be allocated to fund 1-4 new awards, using a cooperative agreement (U01 or U19) mechanism. Eligible institutions include for-profit or non-profit organizations; public or private institutions, such as universities, colleges, hospitals, and laboratories; units of State and local governments; or eligible agencies of the Federal government. Foreign institutions are not eligible to apply as the primary institution, but may enter into a consortium or subcontract with a domestic institution as the primary applicant. Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their

institution to develop an application as the principal investigator. Each applicant may submit only one application as a principal investigator. However, participation in multi-project applications (U19 mechanism) as a subcontractor or project leader is allowed if there is no scientific overlap with the application submitted as principal investigator.

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001), available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

PURPOSE:

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications from single institutions or consortia of institutions to participate in a cooperative research group to define the association between human leukocyte antigen (HLA) region genes or genetic markers and immune-mediated diseases, including risk and severity of disease, and organ, tissue, and cell transplantation outcomes.

The goal of this RFA is to establish a cooperative research group to conduct research and to generate high quality HLA-disease association data for public use that will be submitted to and maintained by dbMHC, the publically accessible database of MHC genetics housed and maintained by the National Center for Biomedical Information (NCBI) at the National Institutes of Health National Library of Medicine (NLM). Analysis of data results and data submission to dbMHC will be performed through the NIAID Bioinformatics Information Support Contract (BISC), which is anticipated to be awarded by September 30, 2004 (see http://www.niaid.nih.gov/contract/archive2002.htm for the most recent RFP solicitation). A Notice in the NIH Guide Notice to Grants and Contracts will be issued shortly after award of the BISC contract and will link interested investigators to a website containing additional information on the contract. Inquiries regarding the BISC contract are to be directed to the NIAID staff contact listed in Section VII Agency Contacts below.

RESEARCH OBJECTIVES:

Background:

The human major histocompatibility complex (MHC) genes, known as human leukocyte antigens (HLA) genes, are located within a 4-megabase span on chromosome 6. The HLA region contains 224 identifiable genes, of which at least 128 are expressed, and more than 50 are involved in the immune response. The HLA genomic region is subdivided into: the HLA Class I region, including the classical HLA-A, -B, and -C genes, and the non-classical HLA-E, -F, and –G genes, which exhibit a lower degree of polymorphism and are expressed on a more restricted set of cells than are the classical HLA Class I genes; the HLA Class II region, including HLA-DR, -DQ, and –DP genes; and the HLA Class III region, which includes a diverse set of genes including those for complement components, inflammatory mediators, and other immune response genes. HLA Class I and II-encoded molecules present endogenously and exogenously derived peptides to T cells. HLA Class I molecules also serve as identification ligands for Killer Immunoglobulin-like Receptors (KIR) on natural killer cells.

The HLA gene complex is the most polymorphic region of the human genome, displaying an extraordinary degree of sequence variation between individuals, racial groups and ethnic populations. For example, more than 550 HLA-B gene alleles have been identified. In addition, investigators have noted intriguing correlations between the presence or absence of particular HLA alleles or haplotypes of alleles and the susceptibility to certain immune-mediated diseases, such as multiple sclerosis and rheumatoid arthritis. Decades of research on HLA gene polymorphisms have provided valuable insights into the role of HLA Class I and II gene disparities between donors and recipients in graft survival. Finally, associations have been demonstrated between immune-mediated disease risk and severity, and between transplant outcomes and polymorphisms in non-antigen-presenting genes encoded within the HLA gene locus (e.g., tumor necrosis factor).

In fiscal year (FY) 2000, NIAID, with co-sponsorship from several NIH institutes and the Juvenile Diabetes Research Foundation International, began support of an integrated research program within the International Histocompatibility Working Group (IHWG). This program consists of research projects addressing the population diversity of the HLA gene complex; the association of genetic markers within the HLA region with autoimmune disease risk and severity; KIR diversity; and the degree of HLA allele donor-recipient matching required for optimum outcomes in hematopoietic stem cell transplantation. Through this large international effort, researchers have discovered new associations between genetic markers within the HLA complex and susceptibility to several autoimmune diseases. Researchers have also identified HLA mismatches, not evident by conventional serological typing, that increase risk for mortality, incidence of severe graft-versus-host disease (GVHD), or graft failure following hematopoietic stem cell transplantation.

One of the major outcomes of the IHWG research program is the development of a publicly accessible database housing the HLA-disease association genetic data. This database, called dbMHC (http://www.ncbi.nih.gov/mhc), was developed in a parallel effort with the NCBI and is continuously updated to provide optimum utilization by scientific and medical professionals and the public.

In March 2004, NIAID convened an expert panel to identify the most pressing scientific questions surrounding the role of HLA genetics in immune-mediated diseases. The focus of the discussion included factors common to multiple diseases, genetic variants, HLA population diversity, and considerations for translating HLA associations to the improvement of clinical outcomes. Despite progress on the role of HLA region genetic factors in disease susceptibility and progression, the panel concluded that continued collaborative work in this area was necessary and recommended the following: encourage the development of a broad-based consortium of researchers interested in studying inter-disease HLA genetics; continue efforts to identify, map, and associate genetic variants with various immune-mediated diseases, with an emphasis on population diversity; and continue populating dbMHC with high quality, high resolution HLA genetics data.

The NIAID Bioinformatics Information Support Contract (BISC) program was developed to provide access for all NIAID-supported investigators to high-quality bioinformatics technology support for projects involving complex data sets that may require special data handling capabilities. The pilot phase was completed in FY 2003, and an award is anticipated in September 2004. BISC is charged with developing progressive standards for data collection, curation, and exchange that can be adapted by NIAID-supported research programs. BISC will provide information technology support, software development, statistical analysis, and appropriate technical guidance for all HLA Region Genetics in Immune-Mediated Diseases Cooperative Research Group awardees. In addition, data submission to dbMHC will be facilitated by BISC. For more details concerning the involvement and responsibilities of BISC, please see COOPERATIVE AGREEMENT TERMS AND CONDITIONS OF AWARD; located in **Section VI 2.A.**

NIAID staff contact information for questions regarding BISC can be found under Section VII Agency Contacts.

Objective and Scope:

This RFA will support prospective and/or retrospective studies to investigate the role of HLA genetics in susceptibility to or protection from immune-mediated diseases, including autoimmune diseases and primary immunodeficiency diseases, GVHD, and graft rejection or survival in solid organ, tissue and cell transplantation. Research projects may address: (1) the association of HLA or KIR genes with susceptibility or resistance to immune-mediated diseases, including autoimmune diseases and primary immunodeficiency diseases (common variable immunodeficiency and IgA deficiency); (2) the correlation of transplant outcome

with the level of donor-recipient HLA and/or KIR match or mismatch at the allele level, determined at a high resolution; (3) the discovery of new HLA complex gene and immune-mediated disease associations; and/or (4) the mechanistic basis of HLA loci-disease associations. The primary focus of the application must be on the correlation between HLA region genetics and immune-mediated diseases and/or transplantation outcomes. Studies examining racial-, ethnic-, or gender-specific HLA region genetic diversity related to disease susceptibility or transplant outcome are especially encouraged. Studies may examine polymorphisms in the coding and/or non-coding regions within the MHC locus. Multi-institutional projects are encouraged to provide the breadth and depth of expertise and research tools necessary to carry out the objectives of this RFA. The applicant will be responsible for all aspects of data collection, determination of optimal sample size for statistical power/validity, and, in collaboration with BISC, statistical analysis of study results (for a complete description of awardee scope responsibilities, see section below entitled COOPERATIVE AGREEMENT TERMS AND CONDITIONS OF AWARD; **located in Section VI 2.A.** Examples of responsive areas of research include, but are not limited to, the following:

- Associations between immune-mediated diseases or transplant outcomes, including solid organ transplantation, and (1) single nucleotide polymorphisms (SNPs) or microsatellites (Msat) within the HLA locus; (2) non-HLA genes within the HLA locus; and/or (3) HLA locus gene dose effects associated with disease severity;
- Studies on the effect of varying degrees of HLA allele matching on outcomes in solid organ transplantation or GVHD in hematopoietic cell transplantation;
- Population studies defining the associations of HLA region polymorphisms and alleles with immune-mediated diseases; and
- HLA genetic and disease associations disproportionately affecting certain racial, ethnic, or gender groups.

Diseases to be studied may include, but are not limited to, the following:

- Graft-versus-Host Disease
- Graft rejection and survival
- Multiple Sclerosis
- Rheumatoid Arthritis
- Systemic Lupus Erythematosis
- Primary Immunodeficiency Diseases (e.g., Common Variable Immunodeficiency and IgA Deficiency)

This RFA will not support:

- Clinical trials; however, applicants may request support for clinical procedures to obtain patient samples provided these procedures and associated costs are strongly justified. Funding will not be approved for patient samples derived from routine patient care or that are a component of any clinical trial protocol
- Serology-based HLA typing projects, unless they are coupled to comparative studies of high-resolution gene-based HLA typing
- Development or analysis of animal models for HLA-related disease associations
- HLA association studies with infectious disease susceptibility or resistance
- Animal studies
- Type 1 Diabetes association studies
- Population diversity studies unless linked directly to immune-mediated disease prevalence or severity studies

Section II. Award Information

1. Mechanism(s) of Support

This funding opportunity will use the U01 single-project and U19 multi-project award mechanism(s). As an

applicant, you will be solely responsible for planning, directing, and executing the proposed project.

This funding opportunity uses just-in-time concepts. It also uses the non-modular budget formats**.**

The NIH (U01 and U19) are cooperative agreement award mechanisms. In the cooperative agreement mechanism, the Principal Investigator retains the primary responsibility and dominant role for planning, directing, and executing the proposed project, with NIH staff being substantially involved as a partner with the Principal Investigator, as described under the section VI. 2. Administrative and National Policy Requirements, "Cooperative Agreement Terms and Conditions of Award".

The total project period for applications submitted in response to the RFA may not exceed five years. At this time, the NIAID has not determined the manner by which the research activities will be continued beyond the present RFA.

2. Funds Available

The NIAID intends to commit approximately $2 million dollars in FY 2005to fund 1-4 new and/or competitive continuation grants in response to this RFA. An applicant may request a project period of up to five years. Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Although the financial plans of the IC(s) provide support for this program, awards pursuant to this RFA are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

You may submit (an) application(s) if your organization has any of the following characteristics:

- For-profit or non-profit
- Public or private institutions, such as universities, colleges, hospitals, and laboratories
- Units of State and local governments
- Eligible agencies of the Federal government
- Foreign institutions are not eligible to apply

Foreign institutions are not eligible to apply as the primary institution, but may enter into a consortium or subcontract with a domestic institution as the primary applicant.

1.B. Eligible Individuals

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

2. Cost Sharing

Not Applicable http://grants.nih.gov/grants/policy/nihgps_2003/nihgps_Part2.htm#matching_or_cost_sharing

3. Other-Special Eligibility Criteria

Not Applicable

Section IV. Application Submission Instructions

1. Address to Request Application Information

The PHS 398 application instructions are available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY 301-451-0088.

2. Content and Form of Application Submission

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). Applications must have a D&B Data Universal Numbering System (DUNS) number as the universal identifier when applying for Federal grants or cooperative agreements. The D&B number can be obtained by calling (866) 705-5711 or through the web site at http://www.dunandbradstreet.com/. The D&B number should be entered on line 11 of the face page of the PHS 398 form.

See also Subsection VI.2. Administrative and National Policy Requirements jp for additional information.

The title and number of this funding opportunity must be typed on line 2 of the face page of the application form and the YES box must be checked.

3. Submission Dates

Special receipt date is listed in Section IV.3.A

3.A. Receipt, Review and Anticipated Start Dates

Letters Of Intent Receipt Date(s): December 10, 2004
Application Receipt Dates(s): January 11, 2005
Peer Review Date(s): April, 2005
Council Review Date(s): June, 2005
Earliest Anticipated Start Date: July, 2005

3.A.1. Letter of Intent

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this funding opportunity

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows IC staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document.

The letter of intent should be sent to:

Dr. Kenneth Santora
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Room Number 3265, MSC 7616
6700-B Rockledge Drive
Bethesda, MD 20892-7616
FEDEX ZIP: 20817-7616
Telephone: (301) 451-2605
FAX: (301) 402-2638
E-mail: ks419i@nih.gov

3.B. Sending an Application to the NIH

Applications must be prepared using the PHS 398 research grant application instructions and forms as described above. Submit a signed, typewritten original of the application, including the checklist, and three signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710 (U.S. Postal Service Express or regular mail)
Bethesda, MD 20817 (for express/courier service; non-USPS service)

At the time of submission, two additional copies of the application and all copies of the appendix material must be sent to:

Dr. Peter Jackson
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Room Number 3140, MSC 7616
6700-B Rockledge Drive
Bethesda, MD 20892-7616
FEDEX ZIP: 20817-7616
Telephone: (301) 496-8426
FAX: (301) 402-2638
E-mail:pj8v@nih.gov

Using the RFA Label: The RFA label available in the PHS 398 application instructions must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at:
http://grants.nih.gov/grants/funding/phs398/label-bk.pdf.

3.C. Application Processing

Applications must be received **on or before the application receipt date** listed in the heading of this funding opportunity. If an application is received after that date, it will be returned to the applicant without review.

The NIH will not accept any application in response to this funding opportunity that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. However, when a previously unfunded application, originally submitted as an investigator-initiated application, is to be submitted in response to a funding opportunity, it is to be prepared as a NEW application. That is, the application for the funding opportunity must not include an Introduction describing the changes and improvements made, and the text must not be marked to indicate the changes from the previous unfunded version of the application.

Although there is no immediate acknowledgement of the receipt of an application, applicants are generally notified of the review and funding assignment within eight (8) weeks.

4. Intergovernmental Review

This initiative is not subject to intergovernmental review

5. Funding Restrictions

Not Applicable

All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm (See also Section VI.3. Award Criteria)

6. Other Submission Requirements

Applicants for U19 grants must follow special application guidelines in the NIAID Brochure entitled INSTRUCTIONS FOR APPLICATIONS FOR MULTI-PROJECT AWARDS; this brochure is available via the WWW at: http://www.niaid.nih.gov/ncn/grants/multibron.htm. Multi-project grant applications must have two or more individual projects and may include scientific cores and an administrative core. Scientific cores must serve at least two individual projects within the multi-project grant. Specific application details for multi-project grant applications are available at http://www.niaid.nih.gov/ncn/grants/multi/3aa.htm.

This brochure presents specific instructions for sections of the PHS 398 (rev. 5/01) application form that should be completed differently than usual. For all other items in the application, follow the usual instructions in the PHS 398.

All applications must include:

1) a clear research plan(s) and project goal(s) to be completed during the award period. The applicant must clearly state the interim objectives and milestones (e.g. subject recruitment and data reporting) to be achieved during the project, identify impediments or critical decision points that could require a revision in the work plan, and provide a detailed timeline for the attainment of each goal;

2) a detailed description of the statistical considerations to be utilized in determining the sample size and statistical power/validity for the proposed studies and a justification for the required sample size for each proposed research project;

3) documentation of the scientific and technical expertise required to design, conduct, and analyze the proposed studies;

4) a description of study populations and, for prospective studies, demonstrated capacity to recruit human subjects. Human samples may be derived from ongoing, completed, or prospective clinical trials or studies in which samples were maintained for the expressed purpose of future genetic research or in which individuals are re-consented to allow use of specimens for this research. Support for clinical procedures to obtain samples that are not part of an associated clinical trial or study (e.g., additional biopsies) must be clearly described and strongly justified. In addition, applications must include documentation of the ability to acquire human samples and clinical data for the proposed studies. The NIH brochure entitled "Research on Human Specimens: Are You Conducting Research Using Human Subjects?" may be useful to applicants (http://www-cdp.ims.nci.nih.gov/policy.html). OHRP guidance on Repositories, Tissue Storage Activities and Data Banks should also be considered (http://www.hhs.gov/ohrp/humansubjects/guidance/reposit.htm). IRB approval of the consent form(s) is not required at the time of submission of the application. However, at a minimum, a draft of

the consent form to be used for the studies must be included, as well as the consent form for any associated clinical trial or study, if applicable.

5) detailed plans for data collection and quality assurance;

6) the name and qualifications of a statistician to serve as a liaison to BISC for interaction throughout the data submission, cleaning, and analysis phases;

7) a clear plan for interacting with BISC through the statistical liaison;

8) an outline of the process and format proposed for data submission to BISC; and

9) written commitment to: serve on the Steering Committee; adhere to the policies and decisions reached by the Steering Committee, including following the consensus data acquisition protocols and adjunct studies; and accept the participation and assistance of NIH staff in accordance with the guidelines discussed in "Cooperative Agreement Terms and Conditions of Award: NIAID Staff Responsibilities."

U19 Applications: Multi-project applications must provide: a clear and concise plan that depicts the interrelationships among the research groups, their relevant experience/expertise, and the contribution of each to fulfillment of the objectives of this RFA; and an organizational chart of the U19 cooperative group showing the name, organization, and scientific discipline of the PI and of all key scientific and technical personnel, as well as a discussion of lines of authority and plans for the coordination of research projects. If the application is from a consortium of institutions, the applicant must provide a plan to assure the maintenance of close cooperation and effective communication among members of the U19 cooperative group.

SPECIAL REQUIREMENTS

Applicants are encouraged to contact NIAID program staff well in advance of the application submission date to discuss the proposed research program. Also this will allow staff to assess responsiveness to this RFA and provide appropriate guidance as needed with regard to this initiative. Discussion with program staff does not guarantee funding of an application.

1. Research Project Milestones/Interim Objectives

All research projects will have defined interim objectives and milestones (e.g., subject recruitment and data reporting) to be achieved during the project period. The awardee's milestones and interim objectives may be provided to the Steering Committee for review of progress. It is anticipated that milestones may require some annual adjustment at the award anniversary dates, both to incorporate the awardee's scientific accomplishments and progress in the field in general, as well as to reflect the recommendations of the Steering Committee.

2. Statistical Requirements

Key personnel for all awards made under this RFA shall include a statistician to serve as the project statistical expert, as liaison to BISC, and as the point of contact between BISC and the Principal Investigator for issues related to the design and implementation of statistical methods utilized by BISC for analysis of study results. Statistical analysis, data archiving, data submission to dbMHC and development of any necessary analytical tools will be the responsibility of BISC with input from the Principal Investigator, statistical liaison, and the Steering Committee (see Cooperative Agreement Terms and Conditions of Award: Data Handling and Statistical Analysis).

3. Participation in the Collaborative Group

Each awardee must participate in the NIAID HLA Region Genetics in Immune-Mediated Diseases Cooperative Research Group (see Cooperative Agreement Terms and Conditions of Award located in **Section VI 2.A.** This

includes participation in two Steering Committee meetings in the first year of the project and annually thereafter. At least one of the meetings in the first year and the subsequent annual meetings will be held in the Bethesda, Maryland area. Budget requests should include travel funds to attend Steering Committee meetings for all Principal Investigators and for one project leader for U19 projects. Statistical liaisons are not required to attend Steering Committee meetings, but may be invited if statistical issues are to be specifically discussed.

Specific Instructions for Modular Grant applications.

Not Applicable

Specific Instructions for Applications Requesting $500,000 (direct costs) or More per Year.

Not Applicable

Plan for Sharing Research Data

The precise content of the data-sharing plan will vary, depending on the data being collected and how the investigator is planning to share the data. Applicants who are planning to share data may wish to describe briefly the expected schedule for data sharing, the format of the final dataset, the documentation to be provided, whether or not any analytic tools also will be provided, whether or not a data-sharing agreement will be required and, if so, a brief description of such an agreement (including the criteria for deciding who can receive the data and whether or not any conditions will be placed on their use), and the mode of data sharing (e.g., under their own auspices by mailing a disk or posting data on their institutional or personal website, through a data archive or enclave). Investigators choosing to share under their own auspices may wish to enter into a data-sharing agreement. References to data sharing may also be appropriate in other sections of the application.

All applicants must include a **plan** for sharing research data in their application. The data sharing policy is available at http://grants.nih.gov/grants/policy/data_sharing. All investigators responding to this funding opportunity should include a description of how final research data will be shared, or explain why data sharing is not possible.

The reasonableness of the data sharing **plan** or the rationale for not sharing research data will be assessed by the reviewers. However, reviewers will not factor the proposed data sharing **plan** into the determination of scientific merit or the priority score.

Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication. NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm and http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part7.htm#_Toc54600131. Investigators responding to this funding opportunity should include a **plan** for sharing research resources addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the data sharing **plan** and the resources sharing **plan** will be considered by Program staff of the funding organization when making recommendations about funding applications. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report. (PHS 2590). See Section VI.3. Award Criteria.

Section V. Application Review Information

1. Criteria

Not Applicable

2. Review and Selection Process

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the NIAID. Incomplete applications will not be reviewed.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the NIAID in accordance with the review criteria stated below.

As part of the initial merit review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score.
- Receive a written critique
- Receive a second level of review by the National Advisory Allergy and Infectious Diseases Council

3. Merit Review Criteria

Applications submitted in response to a funding opportunity will compete for available funds with all other recommended applications.

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. The scientific review group will address and consider each of these criteria in assigning the application's overall score, weighting them as appropriate for each application.

- Significance
- Approach
- Innovation
- Investigator
- Environment
- Additional Review Criteria

The application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

Significance: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

Approach: Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? For prospective studies, is the evidence of successful experience in recruitment and retention of research subjects adequate?

Innovation: Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

Investigator: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

The general review criteria for U19 multi-project cooperative agreement applications are presented in the NIAID brochure entitled "INSTRUCTIONS FOR APPLICATIONS FOR MULTI-PROJECT AWARDS" at http://www.niaid.nih.gov/ncn/grants/multibron.htm.

3.A. Additional Review Criteria:

In addition to the above criteria, the following items will be considered in the determination of scientific merit and the priority score:

Protection of Human Subjects from Research Risk: The involvement of human subjects and protections from research risk relating to their participation in the proposed research will be assessed. See also Section VIII - Other Information.

Inclusion of Women, Minorities and Children in Research: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research will be assessed. Plans for the recruitment and retention of subjects will also be evaluated. See also Section VIII-Other Information .

Care and Use of Vertebrate Animals in Research: If vertebrate animals are to be used in the project, the five items described under Section f of the PHS 398 research grant application instructions (rev. 5/2001) will be assessed.

3.B. Additional Review Considerations

Budget: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

In addition to the above criteria, the following items will be considered in the determination of scientific merit and the priority score:

(1) Adequacy of the proposed plan for roles, responsibilities, and flow of data and other information between project statistical liaison and BISC staff, including the expertise and qualifications of the statistical liaison.

(2) Evaluation of the statistical power analysis utilized to ensure the validity of the sample size.

(3) Evidence of successful experience in recruitment and retention of Human Subjects.

(4) Technical and administrative feasibility of plans to conduct studies with Human Subjects.

3.C. Sharing Research Data

2. **Data Sharing Plan:** The reasonableness of the data sharing **plan** or the rationale for not sharing research data **will** be assessed by the reviewers. However, reviewers will not factor the proposed data sharing plan into the determination of scientific merit or the priority score. The presence of a data sharing **plan** will be part of the terms and conditions of the award. The funding organization will be responsible for monitoring the data sharing policy.

Data Sharing and Submission to dbMHC

Timely release of data to NIH-supported and/or public databases is expected in accordance with the guidelines established by the Steering Committee and the NIH data sharing policy available at: http://grants.nih.gov/grants/policy/data_sharing/ One of the goals of this cooperative research group is to enter all data generated from these studies into the NCBI-maintained dbMHC database (http://www.ncbi.nih.gov/mhc), an open, publicly accessible platform for DNA and clinical data related to the human major histocompatibility complex. All data generated or analyzed through this cooperative group will be submitted to dbMHC through BISC. Data submitted to dbMHC will be released to the public on a schedule determined by the Steering Committee and agreed to by NIAID and the NCBI.

3.D. Sharing Research Resources

NIH policy requires that grant awardee recipients make unique research resources readily available for research purposes to qualified individuals within the scientific community after publication. NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps and http://www.ott.nih.gov/policy/rt_guide_final.html. Investigators responding to this funding opportunity should include a sharing research resources **plan** addressing how unique research resources will be shared or explain why sharing is not possible.

The adequacy of the resources sharing **plan** will be considered by Program staff of the funding organization when making recommendations about funding applications. Program staff may negotiate modifications of the data and resource sharing **plans** with the Principal Investigator before recommending funding of an application. The final version of the data and resource sharing **plans** negotiated by both will become a condition of the award of the grant. The effectiveness of the resource sharing will be evaluated as part of the administrative review of each non-competing Grant Progress Report. (PHS 2590). See Section VI.3. Award Criteria.

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, the Principal Investigator will also receive a written critique called a summary statement.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part4.htm

A formal notification in the form of a Notice of award will be provided to the applicant organization. The notice of award signed by the grants management officer is the authorizing document.

Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NGA (Notice of Grant Award) are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs.

2. Administrative and National Policy Requirements

All NIH Grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the notice of grant award. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part4.htm and Part II Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_part9.htm.

The following Terms and Conditions will be incorporated into the award statement and will be provided to the Principal Investigator as well as to the appropriate institutional official, at the time of award.

2.A. Cooperative Agreement Terms and Conditions of Award

The following special terms of award are in addition to, and not in lieu of, otherwise applicable OMB administrative guidelines, HHS grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement (U01 single-project and U19 multi-project), an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility resides with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

Monitoring Clinical Studies

When clinical studies or trials are a component of the research proposed, NIAID policy requires that studies be monitored commensurate with the degree of potential risk to study subjects and the complexity of the study. AN UPDATED NIAID policy was published in the NIH Guide on July 8, 2002 and is available at: http://grants.nih.gov/grants/guide/notice-files/NOT-AI-02-032.html. The full policy, including terms and conditions of award, is available at: http://www.niaid.nih.gov/ncn/pdf/clinterm.pdf.

2.A.1. Principal Investigator Rights and Responsibilities

The Principal Investigator will have the primary responsibility for: Awardees will have primary responsibility for defining the research objectives, approaches and details of the projects within the guidelines of the RFA and for performing the scientific activity. Specifically, awardees have primary responsibility as described below.
The Principal Investigators will: determine and coordinate the scientific and administrative activities of the approved projects; set project goals and timelines; accept and implement common guidelines approved by the Steering Committee; collect, validate and assure the quality of the data; interact with BISC staff through the statistical liaison; submit data to BISC, and agree to the subsequent submission of these data to dbMHC by BISC in accordance with policies agreed upon and established by the Steering Committee and the NIH data sharing policy available at: http://grants.nih.gov/grants/policy/data_sharing/; attend Steering Committee meetings and serve as a voting member of the Steering Committee; and participate in the cooperative group. The awardee will be responsible for the study design and preliminary statistical analysis necessary to ensure adequate sample size for study validity.

NIAID intends to support the peer-reviewed studies proposed in the awarded grant applications. However, under special circumstances (e.g., duplicative or overlapping specific aims among awardees), the Steering Committee will establish guidelines and review procedures, and will evaluate and recommend to NIAID opportunities for collaboration, redirection or modification of the peer-reviewed or new projects when applicable and necessary. This policy is in keeping with the terms and conditions of the cooperative agreement mechanism. Any recommendations that result in a change in the scope of research projects must be approved by the NIAID Program Official and Grants Management Officer.

Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current HHS, PHS, and NIH policies.

2.A.2. NIH Responsibilities

An NIH Project Scientist will have substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below.

NIAID staff assistance will be provided by a Program Official from the Transplantation Basic Sciences Section, Transplantation Immunobiology Branch, NIAID Division of Allergy, Immunology and Transplantation, or his/her designee, who will serve as the NIAID Scientific Coordinator. The NIAID Scientific Coordinator will have

substantial scientific/programmatic involvement during the conduct of this activity through technical assistance, advice and coordination above and beyond normal program stewardship for grants, as described below.

During performance of the award, the NIAID Scientific Coordinator, with assistance from other scientific program staff who are designated based on the research topic and their relevant expertise, may provide appropriate assistance, advice, and guidance by: participating in the design of the activities; advising in the selection of sources or resources; advising in project management and technical performance; and participating in the preparation of publications for collaborative projects, as appropriate. However, the role of the NIAID Scientific Coordinator will be to facilitate and not to direct the activities. It is anticipated that decisions in all activities will be reached by consensus and the NIAID staff will be given the opportunity to offer input into this process. The manner of reaching this consensus and the final decision-making authority will rest with the Steering Committee.

Additionally, an agency program official or IC program director will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice.

An NIAID Program Official will be assigned to perform normal program stewardship responsibilities for the grants awarded under this RFA, including monitoring program progress and approving changes. The Government, via the NIAID Program Official, will have access to data generated under this Cooperative Agreement and may periodically review the data and progress reports. NIAID staff may use information obtained from the data for the preparation of internal reports on the activities of the study. However, awardees will retain custody of and have primary rights to all data developed under these awards.

Release of each annual funding increment by NIAID will be based on an NIAID review of progress towards achieving the previously agreed upon research goals, interim objectives and milestones. It is recognized that project goals may require revision and re-negotiation during the course of the project period. The NIAID reserves the right to terminate or curtail a study (or any individual award) in the event of a substantial shortfall in participant recruitment, follow-up, data reporting, quality control, or other major breach of the approved project.

2.A.3. Collaborative Responsibilities

Steering Committee

A Steering Committee will serve as the governing board of the HLA Region Genetics In Immune-Mediated Diseases Cooperative Research Group. Each member of the Steering Committee will have one vote. At a minimum, membership of the Steering Committee will include the NIAID Scientific Coordinator, each U01/U19 Principal Investigator, one additional individual project investigator from each U19 award, a member of the NCBI dbMHC development staff, and selected scientists other than the awardees when additional expertise is required for committee breadth and balance. The Steering Committee will appoint additional members by majority vote. In addition, the NIAID may appoint two external scientists to an Advisory Working Group (acting in a scientific advisory capacity to NIAID) and a representative from BISC to the Steering Committee as non-voting members. A Chairperson will be selected by the Steering Committee from among the non-federal Committee members. Subcommittees of the Steering Committee may be established as necessary. Each Steering Committee member will be expected to participate in all meetings and activities, e.g., conference calls and special subcommittees as required, and will be required to accept and implement common guidelines and procedures approved by the Steering Committee. The Steering Committee will meet at least twice the first year and annually thereafter. At least one of the meetings in the first year and the subsequent annual meetings will be in Bethesda, Maryland.

Each full member will have one vote. Awardee members of the Steering Committee will be required to accept and implement policies approved by the Steering Committee.

The Steering Committee or a designated subcommittee will prepare an annual report containing the following information: progress of ongoing and newly-initiated projects; manuscripts published, in press, and in preparation; presentations at regional, national, and international meetings; ongoing and planned interactions

with other NIH-supported research programs; other activities of the group; data submitted to dbMHC and other databases, as applicable; and future plans. The first such report will be submitted to the NIAID Program Official no later than 13 months after the initial Notice of Award, or a time agreed upon by the NIAID Program Official, and yearly thereafter.

The NIAID Scientific Coordinator will schedule the meetings of the Steering Committee and actively assist the Chair in developing the meeting agendas. The NIAID Scientific Coordinator will ensure coordination of the Steering Committee's activities and implementation of its recommendations.

The Steering Committee will:

- Serve as the main governing board;
- Identify scientific opportunities, emerging needs, and impediments;
- Ensure the timely release of data through publication and/or release of data to dbMHC and/or other public databases;
- Develop guidelines for publication of collaborative project results;
- Prepare annual reports;
- Review and provide recommendations for human subjects protection issues as needed;
- Evaluate progress of the research projects and provide guidance to investigators regarding study implementation and conduct;
- Establish policies for data handling and interaction with BISC staff, including protocols and standards for data collection, analysis, and management; and
- Establish and/or approve procedures to integrate the data into a form utilizable for meta-analysis across disease areas.

Subcommittees of the Steering Committee may be established as needed to make recommendations on shared aspects of the cooperative research group, including:

- Recruitment of appropriate diversity in patient ethnicity, race, and gender;
- Inclusion criteria for the immune-mediated diseases under study;
- Collection of relevant phenotypic and/or pathophysiologic sample-associated data; and
- A common set of SNPs and microsatellites, including normalization of microsatellite sizes across instrument platforms

Cooperation with Other NIH-Sponsored Programs

In order to most efficiently utilize research resources and rapidly exchange scientific information to promote HLA genetics research and NIAID objectives, it is anticipated that cooperation or opportunities to collaborate with other NIH funded programs will be initiated in future years and will be coordinated and facilitated by the NIAID Scientific Coordinator.

Data Handling and Statistical Analysis

The data generated by this cooperative group will be submitted to BISC. BISC is designed to manage data integration and statistical analysis, and will serve as a central data repository for NIAID-supported research in immune-mediated diseases, including linkages with high resolution HLA genetics information. Each awardee will collect and ensure the consistency and quality of their data, with assistance from BISC, as needed.

BISC Responsibilities

BISC will be responsible for data receipt, deposition, curation, archive and backup, recovery (as necessary), statistical analysis, and subsequent data deposition into and interface with dbMHC or other appropriate public databases (e.g., dbSNP, Genbank). BISC will develop and disseminate software for all data submission and analysis, and establish customized graphical interfaces for frequent and interactive communication with project

investigators. BISC will also provide statistical software tools for local interim analysis (as needed), and assist with technical support in the collection, submission, and exchange of data primarily through the statistical liaison of each U01/U19 project. BISC will provide feedback to the statistical liaison regarding the quality of data submitted, and will accept data from the project(s) in a variety of formats (such as XML or tab-delimited text files), which will be determined in consultation with the Steering Committee and project statistical liaisons.

Data Sharing and Submission to dbMHC

Timely release of data to NIH-supported and/or public databases is expected in accordance with the guidelines established by the Steering Committee and the NIH data sharing policy available at: http://grants.nih.gov/grants/policy/data_sharing/. One of the goals of this cooperative research group is to enter all data generated from these studies into the NCBI-maintained dbMHC database (http://www.ncbi.nih.gov/mhc), an open, publicly accessible platform for DNA and clinical data related to the human major histocompatibility complex. All data generated or analyzed through this cooperative group will be submitted to dbMHC through BISC. Data submitted to dbMHC will be released to the public on a schedule determined by the Steering Committee and agreed to by NIAID and the NCBI.

2.A.4. Arbitration Process

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to arbitration. An Arbitration Panel composed of three members will be convened. It will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special arbitration procedure in no way affects the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulations 42 CFR Part 50, Subpart D and HHS regulations 45 CFR Part 16.

3. Award Criteria

The following will be considered in making funding decisions:

- Scientific merit of the proposed project as determined by peer review
- Availability of funds
- Relevance of program priorities

4. Reporting

Awardees will be required to submit the PHS Non-Competing Grant Progress Report, Form 2590 annually: http://grants.nih.gov/grants/funding/2590/2590.htm and financial statements as required in the NIH Grants Policy Statement.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

1. Scientific/Research Contacts:

Perry M. Kirkham, Ph.D.
Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases
Room 3045, MSC-6601
6610 Rockledge Drive

Bethesda, MD 20892-6601
Telephone: 301-496-5598
FAX: 301-480-0693
Email: pk138u@nih.gov

Direct questions relating to BISC to:

Cheryl Kraft, M.S.
Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases
Room 3005, MSC-6601
6610 Rockledge Drive
Bethesda, MD 20892-6601
Telephone: 301-496-7551
FAX: 301-480-2381
Email: ck23s@nih.gov

2. Peer Review Contacts:

Dr. Peter Jackson
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Room Number 3140, MSC 7616
6700-B Rockledge Drive
Bethesda, MD 20892-7616
FEDEX ZIP: 20817-7616
Telephone: (301) 496-8426
FAX: (301) 402-2638
E-mail: pj8v@nih.gov

3. Financial or Grants Management Contacts:

Ann Devine
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Room 2114, MSC-7614
6700-B Rockledge Drive
Bethesda, MD 20892-7614
Telephone: 301-402-5601
FAX: 301-480-3780
Email: ad22x@nih.gov

Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:
Recipients of PHS support for activities involving live, vertebrate animals must comply with PHS Policy on Humane Care and Use of Laboratory Animals (http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf), as mandated by the Health Research Extension Act of 1985 (http://grants.nih.gov/grants/olaw/references/hrea1985.htm), and the USDA Animal Welfare Regulations (http://www.nal.usda.gov/awic/legislat/usdaleg1.htm), as applicable.

Human Subjects Protection:

Federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained. http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm.

Data and Safety Monitoring Plan:
Data and safety monitoring is required for all types of clinical trials, including physiologic toxicity, and dose-finding studies (phase I); efficacy studies (Phase II) efficacy, effectiveness and comparative trials (Phase III). Monitoring should be commensurate with risk. The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risks to the participants. (NIH Policy for Data and Safety Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

Sharing Research Data:
Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible.
http://grants.nih.gov/grants/policy/data_sharing

Investigators should seek guidance from their institutions, on issues related to institutional policies, local IRB rules, as well as local, State and Federal laws and regulations, including the Privacy Rule. Reviewers will consider the data sharing plan but will not factor the plan into the determination of the scientific merit or the priority score.

Sharing of Model Organisms:
NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html). At the same time the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding pursuant to the Bayh Dole Act (see the NIH Grants Policy Statement http://grants.nih.gov/grants/policy/nihgps_2003/index.htm). All investigators submitting an NIH application or contract proposal beginning with the October 1, 2004 receipt date, are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

Inclusion of Women And Minorities in Clinical Research:
It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

Inclusion of Children as Participants in Clinical Research:
The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include

them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at http://grants.nih.gov/grants/funding/children/children.htm.

Required Education on the Protection of Human Subject Participants:
NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

Human Embryonic Stem Cells (hESC):
Criteria for federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see http://escr.nih.gov/) It is the responsibility of the applicant to provide in the project description and elsewhere in the application as appropriate, the official NIH identifier(s) for the hESC line(s)to be used in the proposed research. Applications that do not provide this information will be returned without review.

Public Access to Research Data through the Freedom of Information Act:
The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this RFA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

Standards for Privacy of Individually Identifiable Health Information:
The Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002 . The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

URLs in NIH Grant Applications or Appendices:
All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

Healthy People 2010:
The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This RFA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

Authority and Regulations:
This program is described in the Catalogue of Federal Domestic Assistance at http://www.cfda.gov/ in the following citations: No. 93.855, Immunology, Allergy, and Transplantation Research and No. 93.856, Microbiology and Infectious Diseases. Awards are made under authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and administered under NIH grants policies and Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

Department of Health and Human Services

National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892